FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Peripheral and Central Nervous System Drugs Advisory Committee (PCNS) Meeting
FDA White Oak Campus, Building 31, The Great Room (Rm. 1503)
White Oak Conference Center, Silver Spring, Maryland
May 22, 2013

Draft Questions to the Committee

Efficacy

1) For suvorexant, the applicant seeks an indication for the treatment of insomnia characterized by difficulties with sleep onset and/or maintenance. The proposed dosing algorithm includes higher and lower doses for non-elderly and elderly patient populations:

	non-elderly age < 65	elderly age ≥ 65
high dose	40 mg	30 mg
starting dose	20 mg	15 mg

a. **DISCUSSION:** Please discuss whether separate doses are necessary for non-elderly and elderly patient populations.

b. **DISCUSSION:** Please discuss separately the evidence of effectiveness in improving sleep onset and sleep maintenance.

c. **VOTE:** Are these dose ranges effective for the treatment of insomnia characterized by difficulties with sleep onset and/or maintenance?

2) The applicant has submitted data supporting the conclusion that 10 mg is an effective dose. If 10 mg were the recommended initial dose, labeling would include a recommendation to increase the dose, if necessary, to achieve efficacy for an individual patient (if safety of higher doses were considered acceptable). Such labeling could reduce side effects and would be consistent with recent labeling changes for zolpidem products.

a. **DISCUSSION:** Please discuss the pros and cons of the general approach of starting sleep-aid drugs at the lowest dose with a reasonable effect, even if not the full effect.

b. **DISCUSSION:** Please discuss whether the applicant has established that 10 mg is an effective dose.

c. **DISCUSSION:** Please discuss whether 10 mg would be an appropriate recommendation as a starting dose, with labeling that suggests increasing the dose for patients in whom 10 mg is not effective.

d. **DISCUSSION:** If 10 mg has not been adequately established as an effective dose, please discuss whether the applicant should be required to perform additional efficacy studies of the 10 mg dose prior to approval.

3) **DISCUSSION:** The Agency believes that the safe use of hypnotic drugs should incorporate the concept that the lowest effective dose should be used. The exposure-response data suggests doses even lower than 10 mg might be effective in some patients. Please discuss whether the applicant should study safety and efficacy of doses lower than 10 mg.

Safety

4) **VOTE:** The applicant has recommended starting doses of 15 mg and 20 mg in elderly and non-elderly patients, respectively. Is the safety of these doses acceptable?

5) **VOTE:** The applicant has recommended doses up to 30 and 40 mg in elderly and non-elderly patients, respectively, who have not responded to lower doses. Is the safety of these doses acceptable, if recommended only for patients who do not respond adequately to lower doses?

6) **DISCUSSION:** The Agency believes that in some populations (e.g., obese women; patients taking metabolic inhibitors) the 15 mg dose results in excessive suvorexant exposure. Please discuss if you agree.

7) **DISCUSSION:** If you deem the safety of suvorexant to be acceptable at some dose(s), please discuss whether labeling could be adequate to protect patients who drive, and to protect the public? If so, what would need to be included in labeling?